- 83. (Amended) The [milk] method of claim 82, wherein the human polypeptide is lactoferrin.
- 98. (Amended) The method of claim 125, wherein the promoter is [A transgenic bovine having a genome containing a transgene comprising:]
  - a bovine  $\alpha$ -s1 casein promoter; and the enhancer is a
  - a bovine  $\alpha$ -s1 casein enhancer[;
- a secretory DNA sequence encoding a signal sequence functional in bovine mammary secretory cells;
- a recombinant DNA sequence encoding a recombinant polypeptide, the secretory DNA sequence being operably linked to the recombinant DNA sequence, wherein a secretory recombinant DNA sequence is formed, the secretory-recombinant DNA sequence being operably linked to the bovine  $\alpha$ -s1 promoter and enhancer;

wherein the transgene, in a lactating form of the bovine or a female descendant of the bovine, is capable of directing the expression of the secretory-recombinant DNA sequence in bovine mammary secretory cells to produce a form of recombinant polypeptide, that when secreted from the mammary secretory cells produces the recombinant polypeptide in the milk of the bovine or female descendant thereof].

99. (Amended) The [transgenic bovine] method of claim 98, wherein the transgene further comprises:

an  $\alpha$ -s1 casein 3' untranslated sequence.

- 100. (Amended) The [transgenic bovine] method of claim 99, wherein the transgene further comprises an  $\alpha$ -s1 casein 3' flanking sequence.
- 101. (Amended) The [transgenic bovine] method of claim 100, wherein the  $\alpha$ -s1 casein 3' flanking sequence has a length of at least 2 kb.
- 102. (Amended) The [transgenic bovine] method of claim 101, wherein the transgene further comprises at least 16 kb of  $\alpha$ -s1 casein 5' flanking sequence.

- 103. (Amended) The [transgenic bovine] method of claim 102, wherein the transgene further comprises an intronic sequence.
- 104. (Amended) The [transgenic bovine] method of claim 103, wherein the intronic sequence is a hybrid intronic sequence.
- 105. (Amended) The [transgenic bovine] method of claim 104, wherein the hybrid intronic sequence comprises a 5' portion of a bovine  $\alpha$ -S1 casein intronic sequence and a 3' portion of an IgG heavy chain intronic sequence.
- 106: (Amended) The [transgenic bovine] method of claim 105 wherein the 3' portion is a 3' splice signal sequence associated with the J-C segment rearrangement of an IgG heavy chain.
- 107. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a homologous polypeptide from the bovine.
- 108. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a heterologous polypeptide.
- 109. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is selected from the group consisting of human milk proteins, human serum proteins, and industrial enzymes.
- 110. (Amended) The [transgenic bovine] method of claim 109, wherein the heterologous polypeptide is a human milk protein.
- 111. (Amended) The [transgenic bovine] method of claim 110, wherein the human milk protein is selected from the group consisting of secretory immunoglobulins, lysozyme, lactoferrin, lactoglobulin,  $\alpha$ -lactalbumin and bile salt-stimulated lipase.
- 112. (Amended) The [transgenic bovine] method of claim 111, wherein the milk protein is lactoferrin or lysozyme.

- 113. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is a human serum protein.
- 114. (Amended) The [transgenic bovine] method of claim 113, wherein the human serum protein is selected from the group consisting of albumin, immunoglobulin, Factor VIII, Factor IX and Protein C.
- 115. (Amended) The [transgenic bovine] method of claim 114, wherein the serum protein is albumin.
- 116. (Amended) The [transgenic bovine] method of claim 108, wherein the heterologous polypeptide is an industrial enzyme selected from the group consisting of proteases, lipases, chitinases and ligninases.
- 117. (Amended) The [transgenic bovine] method of claim 106, wherein the recombinant polypeptide is a naturally occurring polypeptide.
- 118. (Amended) The [transgenic bovine] method of claim 98, wherein the transgene is the 26 kb NotI fragment of plasmid p26,8hlF4.
- 123. (Amended) A method of producing a transgenic bovine <a href="mailto:species">species</a> the method comprising:

obtaining an ovum from bovine ovaries;

<u>maturing and</u> fertilizing the ovum *in vitro* to form a zygote;

introducing a transgene into the zygote <u>in vitro;</u>

propagating the zygote to form the embryo <u>in vitro;</u> and transplanting the embryo into a recipient female bovine parent, which gestates the embryo to give birth to a transgenic bovine.

125. (Amended) [A transgenic bovine produced by] [t]The method of claim 123 wherein the trangene comprises [having a genome containing a transgene comprising]:

a mammary-gland specific promoter;

a mammary-gland specific enhancer;

a secretory DNA sequence encoding a signal sequence functional in bovine mammary secretory cells;

a recombinant DNA sequence encoding a recombinant polypeptide, the secretory DNA sequence being operably linked to the recombinant DNA sequence, wherein a secretory recombinant DNA sequence is formed, the secretory-recombinant DNA sequence being operably linked to the promoter and enhancer;

wherein the transgene, in a lactating form of the transgenic bovine or a female descendent of the transgenic bovine, is capable of directing the expression of the secretory-recombinant DNA sequence in bovine mammary secretory cells to produce a form of recombinant polypeptide, that when secreted from the mammary secretory cells produces the recombinant polypeptide in the milk of the bovine or female descendent thereof.

126. (Amended) The [transgenic bovine] method of claim [124] 123, wherein the transgene is introduced into the zygote by microinjection.

Please add the following claim.

128. A method of producing an embryo of a transgenic bovine species, comprising:

obtaining an ovum from bovine ovaries;
maturing and fertilizing the ovum in vitro to form a zygote;

introducing a transgene into the zygote, wherein the transgene integrates into the genome of the zygote to form the transgenic embryo.

## <u>Remarks</u>

## **Preliminary**

With the exception of new claim 128, all claims are now dependent directly or indirectly on claim 123. Claim 123 is direct to an *in vitro* method of producing a transgenic bovine species. The claim specifies that steps of maturing an oocyte, fertilizing the oocyte to produce a zygote, introducing a transgene into the zygote and maturing the zygote to an embryo are conducted *in vitro*. Support for the step of maturing an